

Risk factors and genetic polymorphism associated with
susceptibility to obesity

INVENTOR(S): Lapointe, Gilles; Perusse, Louis

PATENT ASSIGNEE(S): Geneob Usa Inc., USA

SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005079325	A2	20050901	WO 2005-US4455	20050214
<p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW</p> <p>RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG</p>				
US 2005191678	A1	20050901	US 2005-56047	20050211
CA 2556177	A1	20050901	CA 2005-2556177	20050214
PRIORITY APPLN. INFO.:				
			US 2004-544087P	P 20040212
			US 2005-56047	A 20050211
			WO 2005-US4455	W 20050214
<p>AB A kit and method for assessing risk factors associated with susceptibility of a subject to a genetically related disease, especially obesity-related diseases,</p> <p>relative to a general population are provided. The risk factors require the inclusion of at least two of age, gender, race, and family history and require the inclusion of a plurality of polymorphisms selected for known correlation with the disease or condition. The risk score is calculated by a risk ratio obtained from the formula $[a/(a+b)] [c/(c+d)]$ multiplied by a constant chosen to place the risk score and base score in comparable units. In the formula, group (a) is a group having both the risk factor and the disease or condition, group (b) has the risk factor and does not have the disease or condition, group (c) does not have the risk factor and has the disease or condition and group (d) does not have the risk factor and does not have the disease or condition. Genetic polymorphisms in gene LEPR, DRD2, HTR2C, MC4R, PPARG, TNFA, FABP2, ADRB2, ADRB3, GRL, UCP2, UCP3, IRS1, SUR1, CAPN10, ACE, AGT, APOE, APOB and LPL are associated with obesity, obesity-related diabetes, obesity-related heart disease.</p>				

L7 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:905909 CAPLUS

DOCUMENT NUMBER: 141:389789

TITLE: Fluorescent labeled probes for detecting human $\beta 3$ adrenaline receptor gene mutation

INVENTOR(S): Hirai, Mitsuharu

PATENT ASSIGNEE(S): Arkray Inc., Japan

SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004092385	A1	20041028	WO 2004-JP5525	20040416
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2004313120	A	20041111	JP 2003-114381	20030418
EP 1616953	A1	20060118	EP 2004-728043	20040416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1809638	A	20060726	CN 2004-80017019	20040416
PRIORITY APPLN. INFO.: JP 2003-114381 A 20030418				
WO 2004-JP5525 W 20040416				

AB Nucleic acid probes and a kit for detecting a mutation in a sequence of $\beta 3$ adrenaline receptor gene substituting tryptophan at the 64-position into arginine (B3AR Trp64Arg mutation) labeled with a fluorescent dye at one end and which shows a decrease in the fluorescence of the fluorescent dye upon hybridization, are provided. Using this nucleic acid probes, the fluorescence of the fluorescent dye is measured by melting curve anal. Based on the results of the melting curve anal., a mutation is detected.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 4 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
 ACCESSION NUMBER: 2004-25926 BIOTECHDS

TITLE: Nucleic acid probe useful for detecting mutation in beta3 adrenaline receptor gene having single nucleotide polymorphism, labeled at terminal with fluorescent dye and shows decrease in fluorescence of fluorescent dye upon hybridization;
 gene mutation detection using DNA primer and DNA probe for use in diagnosis

AUTHOR: HIRAI M
 PATENT ASSIGNEE: ARKRAY INC
 PATENT INFO: WO 2004092385 28 Oct 2004
 APPLICATION INFO: WO 2004-JP5525 16 Apr 2004
 PRIORITY INFO: JP 2003-114381 18 Apr 2003; JP 2003-114381 18 Apr 2003
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 OTHER SOURCE: WPI: 2004-784610 [77]

AN 2004-25926 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - Nucleic acid probe which is labeled at a terminal with a fluorescent dye and which shows a decrease in the fluorescence of the fluorescent dye upon hybridization, comprises a base sequence starting with the base at the 183- position or ending with the base at 196 position of a fully defined sequence of 1227 nucleotides as given in the specification and being labeled at the 3' or 5' end with a fluorescent dye.

DETAILED DESCRIPTION - Nucleic acid probe (I) which is labeled at a terminal with a fluorescent dye and which shows a decrease in the fluorescence of the fluorescent dye upon hybridization, comprises a base sequence starting with the base at the 183-position of a fully defined sequence of 1227 nucleotides as given in the specification, consisting of 8-30 nucleotides and being labeled at

the 5' end with a fluorescent dye, or a base sequence ending with the base at 196-position of a fully defined sequence of 1227 nucleotides as given in the specification, consisting of 7-30 bases and being labeled at the 3' end with a fluorescent dye. An INDEPENDENT CLAIM is also included for a kit (II) for detecting mutation, comprising (I).

BIOTECHNOLOGY - Preferred Probe: (I) comprises any one of the sequences chosen from cgtggccatcgcccggactc, catcgctggactccgagac, catcgctggactccgag, catcgctggactccg and catcgctggactcc. Preferred Kit: (II) further comprises primer for amplifying region containing a mutation of substitution of tryptophan at position 64 of amino acid sequence of beta3 adrenaline receptor into arginine (B3AR Trp64Arg mutation) by using DNA polymerase.

USE - (I) is useful for detecting mutation in beta3 adrenaline receptor gene having single nucleotide polymorphism (SNP) which involves carrying out melting curve analysis by measuring the fluorescence of the fluorescent dye using (I), and detecting the mutation based on the result of melting curve analysis, where the SNPs are mutations of a base sequence in which tryptophan of position 64 of the amino acid sequence of beta3 adrenaline receptor is substituted to arginine (B3AR Trp64Arg mutation). The method further involves obtaining nucleic acid containing the SNPs present in the sample, and amplifying the region containing SNP using DNA polymerase in the presence of (I) (claimed).

ADVANTAGE - (I) is effective in detecting B3AR Trp64Arg mutation within a short time since Tm analysis is completed within seconds. The risk of contamination of the amplified product is prevented, and the process is automated. (31 pages)

L7 ANSWER 4 OF 4 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN

ACCESSION NUMBER: 2004-18138 BIOTECHDS

TITLE: Identifying nucleotide polymorphism, by reacting target nucleic acid with oligonucleotides for wild-type and mutant, labeling either of oligonucleotide, adding nucleic acid specific label and measuring interaction of labels; labeled DNA primer and polymerase chain reaction for polymorphism identification and disease diagnosis

AUTHOR: TAKARADA Y; SOYA Y; KAWAMURA Y

PATENT ASSIGNEE: TOYO BOSEKI KK

PATENT INFO: WO 2004061130 22 Jul 2004

APPLICATION INFO: WO 2002-JP13776 27 Dec 2002

PRIORITY INFO: WO 2002-13776 27 Dec 2002; WO 2002-13776 27 Dec 2002

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

OTHER SOURCE: WPI: 2004-543881 [52]

AN 2004-18138 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - Identifying (M1) nucleotide polymorphism, involves reacting nucleic acid present in sample and containing specific nucleotide polymorphism site with oligonucleotide for wild-type and one or more oligonucleotide for mutants, where one of them is labeled, either simultaneously or separately, adding nucleic acid specific label, and identifying nucleotide polymorphism based on interaction of two labels.

DETAILED DESCRIPTION - Identifying (M1) nucleotide polymorphism, (a) involves reacting nucleic acid sequence (I) present in a sample and containing specific nucleotide polymorphism site with an oligonucleotide (O1) for wild-type and one or more oligonucleotide (O2) for mutants; where at least one of them is labeled, either simultaneously or separately, adding nucleic acid specific label (L1), and identifying nucleotide polymorphism based on interaction of the label of oligonucleotide and (L1), (b) involves making (O1) and (O2) act as primer for (I), performing extension reaction of polymorphism site, adding (L1) which acts on extension product, and identifying nucleotide polymorphism based on interaction of label of oligonucleotide and (L2), or (c)

involves making (O1) and (O2) act as primer for (I), where at least one of them is fluorescent labeled, performing extension reaction of polymorphism site, denaturing the extension products to obtain a single strand, making an oligonucleotide complementary to the extension product to react with it, performing extension of the reaction product to form double stranded nucleic acid, making a double stranded nucleic acid specific fluorescent pigment to act with the above reaction product, and measuring the fluorescence produced by interaction of the two labels. An INDEPENDENT CLAIM is also included for a kit for performing (M1), containing (O1) and one or more (O2), where at least one of them is fluorescent labeled, polymerase, and sample containing nucleic acid specific label.

BIOTECHNOLOGY - Preferred Method: In (M1), (L1) is a fluorescent pigment and is specific for double stranded nucleic acid. The label of oligonucleotide is fluorescent pigment. The interaction between the two labels is fluorescent resonance energy transfer. (M1) involves performing polymorphisms specific amplification reaction using (O1) and (O2) and measuring the interaction between the labels during and/or after the amplification. In (M1b) and (M1c), (I) is amplified beforehand. In (M1c), the first five steps are repeated, amplification is performed and the interaction is measured during and/or after amplification.

USE - (M1) is useful for identifying nucleotide polymorphism (claimed). (M1) is useful for diagnosis of hereditary diseases, life style related diseases such as hypertension, diabetes, etc., and nucleotide polymorphism analysis. (M1) is useful for identifying polymorphism in angiotensin converting enzyme gene, thus diagnosing hypertension.

ADVANTAGE - (M1) does not require complicated detection procedures or expensive labeled probes. (M1) is easily and rapidly carried out without passing through complicated base specific amplification reaction.

EXAMPLE - Polymorphism analysis of 3adrenergic receptor gene was performed by PCR using 3 oligonucleotides namely oligo1, oligo2, and oligo3. Oligo1 had an artificial mismatch (C to A) in wild type nucleic acid sequence, oligo2 had artificial mismatch (C to A) in variant nucleic acid sequence and oligo3 was an antisense strand. DNA was extracted from human leukocyte and nucleotide polymorphism (Trp64Arg) of human 3adrenergic receptor gene was analyzed by PCR using oligo1 and oligo3 which were not labeled, and oligo2 which was labeled by TexasRed. The amplification product was added to a solution of SyberGreen1 and was made to react for 10 minutes at room temperature. The fluorescence intensity was measured with fluorescent plate reader in a dark room. The fluorescence intensity of the sample (FLs1) at 355nm/612nm was calculated using the formula $FLs1 = FLs1 - FLb1$, where FLb1 was blank fluorescent intensity. (14 pages)

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L8 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:961914 CAPLUS
DOCUMENT NUMBER: 143:246206
TITLE: Risk factors and genetic polymorphism associated with
susceptibility to obesity
INVENTOR(S): Lapointe, Gilles; Perusse, Louis
PATENT ASSIGNEE(S): Geneob Usa Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005079325	A2	20050901	WO 2005-US4455	20050214
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2005191678	A1	20050901	US 2005-56047	20050211
CA 2556177	A1	20050901	CA 2005-2556177	20050214
PRIORITY APPLN. INFO.:			US 2004-544087P	P 20040212
			US 2005-56047	A 20050211
			WO 2005-US4455	W 20050214
AB	A kit and method for assessing risk factors associated with susceptibility of a subject to a genetically related disease, especially obesity-related diseases, relative to a general population are provided. The risk factors require the inclusion of at least two of age, gender, race, and family history and require the inclusion of a plurality of polymorphisms selected for known correlation with the disease or condition. The risk score is calculated by a risk ratio obtained from the formula $[a/(a+b)] [c/(c+d)]$ multiplied by a constant chosen to place the risk score and base score in comparable units. In the formula, group (a) is a group having both the risk factor and the disease or condition, group (b) has the risk factor and does not have the disease or condition, group (c) does not have the risk factor and has the disease or condition and group (d) does not have the risk factor and does not have the disease or condition. Genetic polymorphisms in gene LEPR, DRD2, HTR2C, MC4R, PPARG, TNFA, FABP2, ADRB2, ADRB3, GRL, UCP2, UCP3, IRS1, SUR1, CAPN10, ACE, AGT, APOE, APOB and LPL are associated with obesity, obesity-related diabetes, obesity-related heart disease.			

L8 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2004:905909 CAPLUS
DOCUMENT NUMBER: 141:389789
TITLE: Fluorescent labeled probes for detecting
human $\beta 3$ adrenaline receptor gene mutation
INVENTOR(S): Hirai, Mitsuharu
PATENT ASSIGNEE(S): Arkray Inc., Japan
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004092385	A1	20041028	WO 2004-JP5525	20040416
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2004313120	A	20041111	JP 2003-114381	20030418
EP 1616953	A1	20060118	EP 2004-728043	20040416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1809638	A	20060726	CN 2004-80017019	20040416
PRIORITY APPLN. INFO.:			JP 2003-114381	A 20030418
			WO 2004-JP5525	W 20040416

AB Nucleic acid probes and a kit for detecting a mutation in a sequence of $\beta 3$ adrenaline receptor gene substituting tryptophan at the 64-position into arginine (B3AR Trp64Arg mutation) labeled with a fluorescent dye at one end and which shows a decrease in the fluorescence of the fluorescent dye upon hybridization, are provided. Using this nucleic acid probes, the fluorescence of the fluorescent dye is measured by melting curve anal. Based on the results of the melting curve anal., a mutation is detected.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 6 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN

ACCESSION NUMBER: 2004-18138 BIOTECHDS

TITLE: Identifying nucleotide polymorphism, by reacting target nucleic acid with oligonucleotides for wild-type and mutant, labeling either of oligonucleotide, adding nucleic acid specific label and measuring interaction of labels; labeled DNA primer and polymerase chain reaction for polymorphism identification and disease diagnosis

AUTHOR: TAKARADA Y; SOYA Y; KAWAMURA Y

PATENT ASSIGNEE: TOYO BOSEKI KK

PATENT INFO: WO 2004061130 22 Jul 2004

APPLICATION INFO: WO 2002-JP13776 27 Dec 2002

PRIORITY INFO: WO 2002-13776 27 Dec 2002; WO 2002-13776 27 Dec 2002

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

OTHER SOURCE: WPI: 2004-543881 [52]

AN 2004-18138 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - Identifying (M1) nucleotide polymorphism, involves reacting nucleic acid present in sample and containing specific nucleotide polymorphism site with oligonucleotide for wild-type and one or more oligonucleotide for mutants, where one of them is labeled, either simultaneously or separately, adding nucleic acid specific label, and identifying nucleotide polymorphism based on interaction of two labels.

DETAILED DESCRIPTION - Identifying (M1) nucleotide polymorphism, (a) involves reacting nucleic acid sequence (I) present in a sample and containing specific nucleotide polymorphism site with an oligonucleotide (O1) for wild-type and one or more oligonucleotide (O2) for mutants, where at least one of them is labeled, either simultaneously or

separately, adding nucleic acid specific label (L1), and identifying nucleotide polymorphism based on interaction of the label of oligonucleotide and (L1), (b) involves making (O1) and (O2) act as primer for (I), performing extension reaction of polymorphism site, adding (L1) which acts on extension product, and identifying nucleotide polymorphism based on interaction of label of oligonucleotide and (L2), or (c) involves making (O1) and (O2) act as primer for (I), where at least one of them is fluorescent labeled, performing extension reaction of polymorphism site, denaturing the extension products to obtain a single strand, making an oligonucleotide complementary to the extension product to react with it, performing extension of the reaction product to form double stranded nucleic acid, making a double stranded nucleic acid specific fluorescent pigment to act with the above reaction product, and measuring the fluorescence produced by interaction of the two labels. An INDEPENDENT CLAIM is also included for a kit for performing (M1), containing (O1) and one or more (O2), where at least one of them is fluorescent labeled, polymerase, and sample containing nucleic acid specific label.

BIOTECHNOLOGY - Preferred Method: In (M1), (L1) is a fluorescent pigment and is specific for double stranded nucleic acid. The label of oligonucleotide is fluorescent pigment. The interaction between the two labels is fluorescent resonance energy transfer. (M1) involves performing polymorphisms specific amplification reaction using (O1) and (O2) and measuring the interaction between the labels during and/or after the amplification. In (M1b) and (M1c), (I) is amplified beforehand. In (M1c), the first five steps are repeated, amplification is performed and the interaction is measured during and/or after amplification.

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ADVANTAGE - (M1) does not require complicated detection procedures or expensive labeled probes. (M1) is easily and rapidly carried out without passing through complicated base specific amplification reaction.

EXAMPLE - Polymorphism analysis of 3adrenergic receptor gene was performed by PCR using 3 oligonucleotides namely oligo1, oligo2, and oligo3. Oligo1 had an artificial mismatch (C to A) in wild type nucleic acid sequence, oligo2 had artificial mismatch (C to A) in variant nucleic acid sequence and oligo3 was an antisense strand. DNA was extracted from human leukocyte and nucleotide polymorphism (Trp64Arg) of human 3adrenergic receptor gene was analyzed by PCR using oligo1 and oligo3 which were not labeled, and oligo2 which was labeled by TexasRed. The amplification product was added to a solution of SyberGreen1 and was made to react for 10 minutes at room temperature. The fluorescence intensity was measured with fluorescent plate reader in a dark room. The fluorescence intensity of the sample (FLs1) at 355nm/612nm was calculated using the formula $FLs1 = FLs1 - FLb1$, where FLb1 was blank fluorescent intensity. (14 pages)

L8 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:435383 CAPLUS

DOCUMENT NUMBER: 139:18342

TITLE: Collections of transgenic animal lines with subsets of cells characterized by expression of an endogenous marker gene and uses

INVENTOR(S): Serafini, Tito Andrew

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 77 pp., Cont.-in-part of U.S. Ser. No. 783,487.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003106074	A1	20030605	US 2002-77025	20020214
US 2003051266	A1	20030313	US 2001-783487	20010214
PRIORITY APPLN. INFO.:			US 2001-783487	A2 20010214

AB Collections of transgenic animals in which a transforming expression cassette is integrated, either at random or by homologous recombination, in a number of sites across the genome are described. The animals are transformed with a dicistronic expression cassette that includes a marker gene that can be used to characterize the animal and a selectable or screenable marker such as an antibiotic resistance. The two genes are coexpressed, e.g. by using a single promoter and an internal ribosome entry site. Such transgenic animals can then be used to detect, isolate and/or select pure populations of cells having a particular functional characteristic. The isolated cells have uses in gene discovery, target identification and validation, genomic and proteomic anal., etc.

L8 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:637801 CAPLUS

DOCUMENT NUMBER: 137:180780

TITLE: Collections of transgenic animal lines in which a subset of cells characterized by expression of an endogenous "characterizing" gene and uses

INVENTOR(S): Serafini, Tito Andrew

PATENT ASSIGNEE(S): Renovis, Inc., USA

SOURCE: PCT Int. Appl., 170 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064749	A2	20020822	WO 2002-US4765	20020214
WO 2002064749	A3	20030320		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2003051266	A1	20030313	US 2001-783487	20010214

PRIORITY APPLN. INFO.:

US 2001-783487 A 20010214

AB The invention provides lines of transgenic animals, preferably mice, in which a subset of cells characterized by expression of a particular endogenous gene (a "characterizing gene") expresses, either constitutively or conditionally, a "system gene," which preferably encodes a detectable or selectable marker or a protein product that induces or suppresses the expression of a detectable or selectable marker (e.g., the protein product is a transcription factor and the expression of the detectable or selectable marker, or suppression thereof is dependent upon the transcription factor, for example, the nucleotide sequence encoding the detectable or selectable marker is operatively linked to a regulatory element recognized by the system gene product) allowing detection, isolation and/or selection of the subset of cells from the other cells of the transgenic animal, or explanted tissue thereof. In a preferred

embodiment, the transgene introduced into the transgenic animal includes at least the coding region sequences for the system gene product operably linked to all or a portion of the regulatory sequences from the characterizing gene such that the system gene has the same pattern of expression within the animal (i.e., is expressed substantially in the same population of cells) or within the anatomical region containing the cells to be analyzed as the characterizing gene. The invention provides collections of such lines of transgenic animals and vectors for producing them, and also provides methods for the detection, isolation and/or selection of a subset of cells expressing the marker gene in such transgenic animal lines. The vector (preferably a BAC) comprising the system gene coding sequences and characterizing gene sequences is then introduced into the genome of a potential founder animal to generate a line of transgenic animals. Also, preferably, the transgene containing the system gene coding sequences and characterizing gene sequences is present in the genome at a site other than where the endogenous characterizing gene is located. Such transgenic animals can then be used to detect, isolate and/or select pure populations of cells having a particular functional characteristic, preferably cells of the nervous system. Creation of transgenic mouse line expressing a 5HT2A receptor BAC was demonstrated. The isolated cells have uses in gene discovery, target identification and validation, genomic and proteomics anal., etc.

L8 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2002:652980 CAPLUS

DOCUMENT NUMBER: 138:83957

TITLE: Highly multiplexed genotyping of coronary artery disease-associated SNPs using MALDI-TOF mass spectrometry

AUTHOR(S): Nakai, Kenji; Habano, Wataru; Fujita, Takeshi; Nakai, Keiko; Schnackenberg, Joerg; Kawazoe, Kohei; Suwabe, Akira; Itoh, Chuichi

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AB Highly multiplexed genotyping methods are needed to support a comprehensive anal. of single nucleotide polymorphisms (SNPs) in coronary artery disease (CAD)-related genes. In this study we evaluated chip-based MALDI-TOF mass spectrometry for multiplexed genotyping of SNPs associated with CAD. Our anal. included 14 healthy Japanese individuals and 19 Japanese patients with myocardial infarction whose first attack occurred before age 50. We selected 29 candidate genes involved in (1) the renin-angiotensin system, (2) lipid metabolism, (3) cytokines and adhesion mols., (4) growth factors, and (5) the coagulation-fibrinolysis system. Genotyping of candidate SNPs was performed by MALDI-TOF MS using a MassARRAY system, and 4-plex anal. was achieved at a maximum All 39 SNPs determined by the fluorescent dye-terminator cycle sequencing method from four randomly selected patients were found to be in complete agreement with the results obtained from MassARRAY system. Significant differences were observed in the -1965delG of PAI1 (SERPINE1) with respect to allelic frequency, the G>A in the promoter region SNP in SM22 (TAGLN) for dominant genotype, and in two other SNPs (C>T in intron 1 of HGF, and -1965delG of PAI1) for recessive genotype. Three SNPs (803T>C of AGT, 677C>T of MTHFR, 190T>C of ADRB3) showed weak differences in allelic frequency. MALDI-TOF-MS provided high performance with a multiplex assay design for anal. of CAD-related SNPs by increasing the throughput while maintaining a high level of accuracy.

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FILE CONTAINS CURRENT INFORMATION.
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Identifying nucleotide polymorphism, by reacting target
nucleic acid with oligonucleotides for wild-type and mutant,
labeling either of oligonucleotide, adding nucleic acid
specific label and measuring interaction of labels;
labeled DNA primer and polymerase chain reaction
for polymorphism identification and disease diagnosis

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PATENT ASSIGNEE: TOYO BOSEKI KK
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AN 2004-18138 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - Identifying (M1) nucleotide polymorphism, involves reacting nucleic acid present in sample and containing specific nucleotide polymorphism site with oligonucleotide for wild-type and one or more oligonucleotide for mutants, where one of them is labeled, either simultaneously or separately, adding nucleic acid specific label, and identifying nucleotide polymorphism based on interaction of two labels.

DETAILED DESCRIPTION - Identifying (M1) nucleotide polymorphism, (a) involves reacting nucleic acid sequence (I) present in a sample and containing specific nucleotide polymorphism site with an oligonucleotide (O1) for wild-type and one or more oligonucleotide (O2) for mutants, where at least one of them is labeled, either simultaneously or separately, adding nucleic acid specific label (L1), and identifying nucleotide polymorphism based on interaction of the label of oligonucleotide and (L1), (b) involves making (O1) and (O2) act as primer for (I), performing extension reaction of polymorphism site, adding (L1) which acts on extension product, and identifying nucleotide polymorphism based on interaction of label of oligonucleotide and (L2), or (c) involves making (O1) and (O2) act as primer for (I), where at least one of them is fluorescent labeled, performing extension reaction of polymorphism site, denaturing the extension products to obtain a single strand, making an oligonucleotide complementary to the extension product to react with it, performing extension of the reaction product to form double stranded nucleic acid, making a double stranded nucleic acid specific fluorescent pigment to act with the above reaction product, and measuring the fluorescence produced by interaction of the two labels. An INDEPENDENT CLAIM is also included for a kit for performing (M1), containing (O1) and one or more (O2), where at least one of them is fluorescent labeled, polymerase, and sample containing nucleic acid specific label.

BIOTECHNOLOGY - Preferred Method: In (M1), (L1) is a fluorescent pigment and is specific for double stranded nucleic acid. The label of oligonucleotide is fluorescent pigment. The interaction between the two labels is fluorescent resonance energy transfer. (M1) involves performing polymorphisms specific amplification reaction using (O1) and (O2) and measuring the interaction between the labels during and/or after the amplification. In (M1b) and (M1c), (I) is amplified beforehand. In (M1c), the first five steps are repeated, amplification is performed and the interaction is measured during and/or after amplification.

USE - (M1) is useful for identifying nucleotide polymorphism (claimed). (M1) is useful for diagnosis of hereditary diseases, life style related diseases such as hypertension, diabetes, etc., and nucleotide polymorphism analysis. (M1) is useful for identifying polymorphism in angiotensin converting enzyme gene, thus diagnosing hypertension.

ADVANTAGE - (M1) does not require complicated detection procedures or expensive labeled probes. (M1) is easily and rapidly carried out without passing through complicated base specific amplification reaction.

EXAMPLE - Polymorphism analysis of 3adrenergic receptor gene was performed by PCR using 3 oligonucleotides namely oligo1, oligo2, and oligo3. Oligo1 had an artificial mismatch (C to A) in wild type nucleic acid sequence, oligo2 had artificial mismatch (C to A) in variant nucleic acid sequence and oligo3 was an antisense strand. DNA was extracted from human leukocyte and nucleotide polymorphism (Trp64Arg) of human 3adrenergic receptor gene was analyzed by PCR using oligo1 and oligo3 which were not labeled, and oligo2 which was labeled by TexasRed. The amplification product was added to a solution of SyberGreen1 and was made to react for 10 minutes at room temperature. The fluorescence intensity was measured with fluorescent plate reader in a dark room. The fluorescence intensity of the sample (FLs1) at 355nm/612nm was calculated using the formula $FLs1 = FLs1 - FLb1$, where FLb1 was blank fluorescent intensity. (14 pages)